Transfer of pathogens to and from patients, healthcare providers, and medical devices during care activity-a systematic review and meta-analysis

Wolfensberger, Aline ; Clack, Lauren ; Kuster, Stefan P ; Passerini, Simone ; Mody, Lona ; Chopra, Vineet ; Mann, Jason ; Sax, Hugo

Abstract: OBJECTIVE The transfer of pathogens may spread antimicrobial resistance and lead to healthcare-acquired infections. We performed a systematic literature review to generate estimates of pathogen transfer in relation to healthcare provider (HCP) activities. METHODS For this systematic review and meta-analysis, Medline/Ovid, EMBASE, and the Cochrane Library were searched for studies published before July 7, 2017. We reviewed the literature, examining transfer of pathogens associated with HCP activities. We included studies that (1) quantified transfer of pathogens from a defined origin to a defined destination surface; (2) reported a microbiological sampling technique; and (3) described the associated activity leading to transfer. For studies reporting transfer frequencies, we extracted data and calculated the estimated proportion using Freeman-Tukey double arcsine transformation and the DerSimonian-Laird random-effects model. RESULTS Of 13,121 identified articles, 32 were included. Most articles (n=27, 84%) examined transfer from patients and their environment to HCP hands, gloves, and gowns, with an estimated proportion for transfer frequency of 33% (95% confidence interval [CI], 12%-57%), 30% (95% CI, 23%-38%) and 10% (95% CI, 6%-14%), respectively. Other articles addressed transfer involving the hospital environment and medical devices. Risk factor analyses in 12 studies suggested higher transfer frequencies after contact with moist body sites (n=7), longer duration of care (n=5), and care of patients with an invasive device (n=3). CONCLUSIONS Recognizing the heterogeneity in study designs, the available evidence suggests that pathogen transfer to HCPs occurs frequently. More systematic research is urgently warranted to support targeted and economic prevention policies and interventions.

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Review

Transfer of pathogens to and from patients, healthcare providers, and medical devices during care activity—a systematic review and meta-analysis

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Abstract

Objective: The transfer of pathogens may spread antimicrobial resistance and lead to healthcare-acquired infections. We performed a systematic literature review to generate estimates of pathogen transfer in relation to healthcare provider (HCP) activities.
Methods: For this systematic review and meta-analysis, Medline/Ovid, EMBASE, and the Cochrane Library were searched for studies published before July 7, 2017. We reviewed the literature, examining transfer of pathogens associated with HCP activities. We included studies that (1) quantified transfer of pathogens from a defined origin to a defined destination surface; (2) reported a microbiological sampling technique; and (3) described the associated activity leading to transfer. For studies reporting transfer frequencies, we extracted data and calculated the estimated proportion using Freeman-Tukey double arcsine transformation and the DerSimonian-Laird random-effects model.
Results: Of 13,121 identified articles, 32 were included. Most articles (n = 27, 84%) examined transfer from patients and their environment to HCP hands, gloves, and gowns, with an estimated proportion for transfer frequency of 33% (95% confidence interval [CI], 12%–57%), 30% (95% CI, 23%–38%) and 10% (95% CI, 6%–14%), respectively. Other articles addressed transfer involving the hospital environment and medical devices. Risk factor analyses in 12 studies suggested higher transfer frequencies after contact with moist body sites (n = 7), longer duration of care (n = 5), and care of patients with an invasive device (n = 3).
Conclusions: Recognizing the heterogeneity in study designs, the available evidence suggests that pathogen transfer to HCPs occurs frequently. More systematic research is urgently warranted to support targeted and economic prevention policies and interventions.

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Transmission of pathogens to and from patients is associated with the spread of antimicrobial resistance and healthcare-associated infections. Transmission usually occurs indirectly via healthcare providers (HCPs) or via mobile or immobile fomites.[1] Hands are universally recognized as the most important vector,[2] but equipment (eg, stethoscopes) may also act as a vector for pathogen transfer.[3] For successful transfer, pathogens must first be transmitted from a surface of origin (eg, a patient) to an intermediate surface (ie, a vector) and must then survive there long enough to be finally transmitted to the next patient or to the next intermediate vector.[4] The likelihood of transfer depends on multiple factors, including number and type of pathogens present, surface structure,[5] contact time, lag time,[6] humidity,[7] and pressure.[8]

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A patient encounters many different HCPs during a stay in a healthcare institution. Each patient is visited by a median of 3.5 HCPs per hour, mostly nurses, for a median of 3 minutes per visit. The patient environment, intact skin, and body fluids are touched in 33%, 27%, and 18% of visits, respectively.[9] If infection prevention measures are not followed, each contact poses a risk of pathogen transfer.

Prevention policies such as standard and isolation precautions, particularly hand hygiene and the use of gloves and gowns, aim to prevent pathogen transmission.[10] Detailed understanding of transmission dynamics during patient care, however, is pivotal to tailoring preventive measures and policies. To date, no systematic review has addressed the extent to which HCP behavior results in transfer of pathogens.

Therefore, we performed a systematic review and meta-analysis (1) to summarize and describe the current knowledge on pathogen transfer associated with care activity, including the frequency and quantity of pathogen transfer between patients, environmental surfaces, HCPs, their clothing, and medical devices, and (2) to identify the factors associated with increased transmission risk.

Methods

Data sources and searches

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) recommendations when conducting this systematic review.[11] We searched Medline/Ovid, EMBASE and the Cochrane Library using a combination of subject headings and free text search terms (see Appendix: Search Strategy). Studies published before July 7, 2017 in English, French, and German were included. Additional articles were identified by a reference list search of articles included in full text review.

Study selection

We retained studies that met the following criteria:

1. The study occurred in a defined healthcare setting (eg, inpatient and outpatient settings of hospitals, nursing homes, and medical practices) and included common behavior in healthcare institutions (eg, handshakes, physical examinations, and phone calls).
2. The study reported transfer of bacteria, viruses, or fungi by contact from a defined origin surface to a defined destination surface through quantification of contamination by frequency (ie, percentage of contaminated destination surfaces) or by quantity (ie, colony forming units (CFU) on destination surface).
3. The HCP activity associated with pathogen transfer was described.
4. Transfer to destination surface was ascertained by genomic or pulsed-field gel electrophoresis typing of the pathogen or ascertaining a sterile destination surface.
5. Origin and destination surfaces were either the patient's body sites; surfaces in the patient's immediate environment; critical, semicritical, or noncritical medical devices; or HCP body sites, attire, or personal protective equipment.
6. The microbiological sampling method (eg, contact plate, swab, or glove juice method[12]) was accurately described.

We excluded studies reporting laboratory simulations or using artificial contamination or tracers to evaluate transfer. We also excluded investigations of transfer by droplet or airborne route and pathogen transfer during surgical procedures.

One researcher (A.W.) screened all titles and abstracts for potentially relevant studies. To check interrater reliability, 2 independent researchers (L.C. and S.P.) screened a subset of titles and abstracts, then 2 authors (A.W. and L.C.) independently reviewed the full texts of all potentially eligible articles. Discrepancies regarding eligibility were resolved by consensus or by decision of a third reviewer (H.S.).

Data extraction and quality assessment

Using a standardized template, the following variables were abstracted: study setting, microorganism transferred, 'origin' surface (surface from which pathogen was transferred), 'destination' surface (surface to which pathogen was transferred), interaction (activity) leading to transfer, number of interactions, frequency of transfer (percentage of positive destination surfaces), quantity of transfer (number of transferred CFU), and microbiological sampling method. All retained articles were assessed for quality using the Downs and Black checklist,[13] which was modified to fit the noninterventional characteristics of included studies (Appendix Table 1).

Data synthesis and analyses

For studies reporting raw transfer frequency data, rates were calculated by dividing the number of positive destinations by the total number of exposed destination surfaces. The Freeman-Tukey double arcsine transformation for data with a binomial distribution was applied to stabilize the variances. Transformed proportions were pooled using random-effects meta-analysis with exact confidence intervals, and results were displayed in forest plots. All meta-analyses were conducted using the *metaprop* command in Stata software. Also, 2 studies that did not report raw rates were excluded from meta-analysis but were retained in the systematic review.[14,15] An a priori subgroup analysis was performed for studies examining pathogenic bacteria examining destination surface, surface of origin, HCP behavior (standardized vs nonstandardized), microorganism, and microbiological sampling method. Studies that reported transfer quantities and risk factor analysis were not pooled, and the findings are summarized descriptively.

Data synthesis was done using Stata version 13.1 software (StataCorp, College Station, TX). Statistical heterogeneity was initially inspected graphically (forest plot); the degree of heterogeneity was quantified using the I^2 statistic. We defined heterogeneity as $I^2 > 60\%$. Subgroup analyses for differences between subgroups were foreseen if the criterion for heterogeneity was not met. *P* values $< .05$ were considered statistically significant. This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[16]

Results

After removal of duplicates, 13,121 articles were identified by database and manual reference search. We excluded 12,932 articles after title and abstract screening. Interrater reliability of title and abstract screening of a subset of articles (n = 2,000) calculated using the Cohen κ was 0.85 (CI 95%, 0.75–0.94) indicating excellent interrater agreement.[17] After full-text reviews of 189 articles, 32 articles (17%) met eligibility criteria and were included in the overall review (Fig. 1).

Tables 1–3 detail the study characteristics. All studies were conducted in high-income settings. The sample size ranged from 3 to several hundred (mean, n = 124). Surface of origin was the patient or his environment in 94% of the studies (n = 30). Also, 1 study dealt with telephones as the surface of origin,[18] and 1 dealt with the patient environment exclusively.[19] Common destination surfaces were hands (n = 18, 56%), gloves (n = 15, 47%), and gowns or uniforms (n = 7, 22%). Rarely, surfaces such as ultrasound probes,[20,21] stethoscopes,[4,22,23] or the patient and his environment were evaluated as destination surfaces.[14,24] Overall, 30 articles (94%) reported transfer frequency, 9 (28%) reported transfer quantity. Transferred pathogens were bacteria in all but 3 articles: 1 article each focused on dermatophytes, 1 on human papillomavirus (HPV), and 1 on both fungi and bacteria. A multitude of clinical care activities were studied, ranging from a brief touch or handshake to well-defined care tasks (eg, dressing change) to more complex medical or nursing activity (eg, morning care). In 31% of studies (n = 10), the interaction was standardized by role playing with real patients.

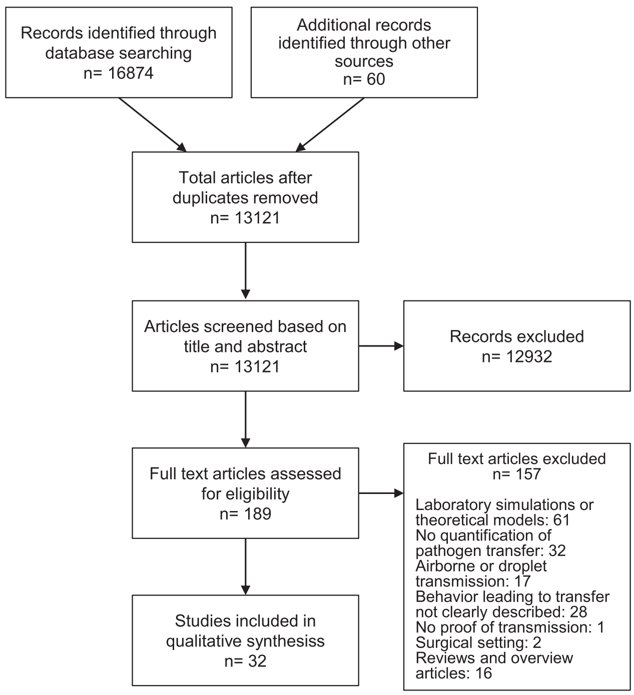

Fig. 1. Study inclusion flow diagram.

Various microbiological sampling techniques were used. Swabbing was applied in 12 studies (38%), contact plates in 14 studies (44%), the glove juice method in 4 studies (13%),[12] and washing hands or gloves in broth in 3 studies (9%). Polymerase chain reaction (PCR) was used to detect viral transfer in 1 study.

Transfer frequency

Most studies examined transfer frequency during nonstandardized tasks, that is, in real-life situations ($n = 23$, 76%) (Table 1). These interactions lasted up to 4 hours. In 8 studies, the transfer frequency after standardized interactions was examined. In 6 of these studies, interactions were simple, such as a handshake, briefly touching a patient, or taking a phone call. In 2 studies, the transfer frequency after multistep interactions, such as an outpatient consultation or a radiology procedure, was examined. Hand and glove contamination ranged from 0% with vancomycin-resistant enterococci (VRE) after a standardized mock radiology procedure[25] to 100% with HPV after treatment of urethral warts.[26] Gown contamination was between 2% and 37% for VRE, methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant (MDR) *Pseudomonas aeruginosa* and *Acinetobacter baumanii*,[22,25,27–30] and 100% for staphylococci.[31] Ultrasound probes were contaminated to 100% with skin bacteria,[20,21] transfer of undifferentiated bacteria to IV stopcocks and syringes occurred in 5%–26% of anesthesia procedures.[32,33]

The pooled proportions of transfer frequency of bacteria to hands and gloves were 33% (95% CI, 12%–57%; 9 studies) and 30% (95% CI, 23%–38%; 21 studies) with overall heterogeneities of $I^2 = 90.95\%$ and 92.03%, respectively (Appendix Fig. 1). The estimated proportions of transfer frequency to gowns and to 'hands after glove removal' were 10% (95% CI, 6%–14%; 13 studies) and 3% (95% CI, 1%–5%; 9 studies), respectively (Appendix Figs. 2 and 3). These results remained unchanged when performing a sensitivity analysis including only studies with a quality score of 100% (Appendix Figs. 4–6). Estimated transfer frequencies stratified according to type of behavior (ie, standardized vs nonstandardized), surface of origin, microorganism, and microbiological sampling method are displayed in Appendix Figs. 7–10.

Figures 2 and 3 provide an overview of transfer frequency for the 2 most commonly evaluated pathogens, VRE and MRSA, depending on origin and destination surfaces.

Transfer quantity

The burden of contamination from pathogen transfer was reported in 9 studies (Table 2). Eight authors reported CFU counts of 10–1000 transferred to 5 fingertips or to the hand. Only 1 study reported considerably higher CFU counts of up to 2×10^6 related to 'moist interactions.'[34]

Risk factor analysis

Behavior leading to contamination was identified by 12 authors through univariable or multivariable analysis (Table 3). Among the studies, 5 identified 'duration of care' as a risk factor for higher frequency of contamination.[2,28,29,35,36] Furthermore, 7 authors described 'contact with moist body sites or invasive devices' (eg, wounds and ventilators) as a risk factor for contamination,[25,28–30,35–37] and 3 authors described the sheer 'presence of an invasive device' (eg, urinary catheter, tracheostomy, and ileostomy).[22,25,37]

Quality of included articles

Quality scores of the studies ranged from 60% to 100% (Tables 1–3), with a mean of 88% and median of 90%. Overall, 26 articles scored >80%, 1 scored 60%,[14] 2 scored 70%,[15,34] and 3 scored 80%.[18,32,38] Appendix Table 1 displays the proportion of studies meeting each quality item. The most common reasons for poor scores included failing to report estimates of the random variability in the data ($n = 19$, 59%) and colonization status of the surface of origin ($n = 10$, 31%).

Discussion

This systematic review on the frequency and quantity of pathogen transfer associated with HCP activities shows substantial variability in studied settings, pathogens, and care activities, as well as application of diverse microbiologic sampling methods. Most studies focused on transfer *from* patients and their environment to HCP hands and gloves, whereas only 2 investigated the transfer from HCP *to* patients. Despite this variability, the following statements have been substantiated: (1) Transfer of pathogens between patients or their environments and HCP or medical devices occurs frequently during patient care, with transfer to hands and gloves occurring more often than transfer to gowns. (2) Higher frequencies of transfer are associated with moist body sites, invasive devices, and longer duration of care. (3) Higher CFU counts are found in contacts with moist surfaces.

Hands are commonly cited as the main vector for transfer of pathogens in the hospital.[39] Gloved hands also act as vectors if gloves are not changed according to guidelines or hands are not disinfected after glove use. In 2006, Pittet et al[40] provided an evidence-based model for hand transmission during patient care and identified 5 steps in patient-to-patient pathogen transmission via HCP hands: (1) organisms present on patients' skin or

Table 1. Summary and Quality Assessment for Studies Reporting Frequency of Contamination

Author (Year of Publication) Quality Score	Microorganism	Study Setting	Standardized vs Nonstandardized Interactions[a]	Interactions (Behavior)	Origin Surface[b]	Destination Surface[c]	Sample Size	Frequency of Contamination After Interaction	Microbiological Sampling Method
Bache et al (2013)[31] Score: 91%	*Staphylococci*	Burns ICU (UK)	Nonstandardized	Dressing change with or without making bed	Patients and their environment (colonization status unknown)	Gowns	24	100%	Contact plate
Boyce et al (1997)[45] Score: 90%	MRSA	Hospital (USA)	Nonstandardized	1) Morning care 2) Nursing activities without patient contact	Patients with MRSA and/or their environment	Gloves	1) 12 2) 12	1) 58% 2) 42%	Swab on agar and swab in broth
Casewell et al (1977)[50] Score: 80%	*Klebsiella*	ICU (UK)	Nonstandardized	Broad spectrum of patient activities (from touching hand to extubation)	Patients with *Klebsiella* and their environment	Hands	47	36%	Glove juice
Duckro et al (2005)[24] Score: 90%	VRE	ICU (USA)	Nonstandardized	Routine patient care	Patients with VRE and their environment	VRE-negative surfaces of patients with VRE and their environment	27	11% (2 steps transfer - via hands or gloves)	Swab in broth
Frazee et al (2011)[20] Score: 90%	1) Undifferentiated bacteria 2) Clinically relevant pathogens	Emergency department (USA)	Nonstandardized	Performing ultrasonography of infection body site	Patients with skin and soft tissue infection (colonization status unknown)	Ultrasound probe	20	1) 100% 2) 70% (MRSA, MSSA, or Streptococci)	Contact plate and swab in broth
Grabsch et al (2006)[27] Score: 90%	VRE	Dialysis ward (Australia)	Nonstandardized	Hemodialysis session (4 hours)	Patients with VRE and their environment	Gowns Gloves Hands	26	Gowns: 30% Gloves: 8% Hands: 8%	Contact plate Glove juice
Grabsch et al (2006)[27] Score: 90%	VRE	1) Outpatient consultation 2) Radiology rooms (Australia)	Standardized	1) Standardized mock outpatient consultation (25 min) 2) Standardized mock radiology procedure (15 min)	Patients with VRE and their environment	Gowns Gloves Hands	1) 25 2) 24	Gowns: 1) 20%, 2) 4% Gloves: 1) 16% Hands: 1) 4%, 2) 0%	Contact plate or Glove juice
Grunwald et al (2015)[51] Score: 90%	Dermatophytes	NA (Israel)	Standardized	Brief touch	Children with tinea	Hands	90	80%	Contact plate
Guerrero et al (2012)[46] Score: 100%	*C. difficile*	NA (USA)	Standardized	Touch 1) Commonly examined skin sites (arm, abdomen, chest, and hand) 2) Environment (table, phone, bedrail, and call button)	Patients with *Clostridium difficile* or their environment	Moistened gloves	30	1) 50% 2) 50%	Contact plate
Hamburger et al (1947)[52] Score: 90%	*Beta-hemolytic streptococci*	NA (USA)	Standardized	Handshake	Sailors with *beta-hemolytic streptococci* 1) Hands after nose blowing 2) Hands without blowing nose	Hands	1) 17 2) 9	1) 76% 2) 66%	"Wash" hands in broth
Hayden et al (2008)[43] Score: 100%	VRE	ICU (USA)	Nonstandardized	1) Patient care with touching patient and environment 2) Patient care with touching environment only	Patients with VRE and/or their environment	Hands Gloves	1) 59 (4 hands, 55 gloves) 2) 44 (15 hands, 29 gloves)	1) Hands: 75% Gloves: 69% 2) Hands: 27% Gloves: 66%	Glove juice

Heid et al (2016)[53] Score: 82%	Undifferentiated bacteria	Operating room and postanesthetic care unit (Germany)	Nonstandardized	Preparation of syringe, and anesthetic management of single patient with either: 1) Syringes capped with new syringe cap from a sterile wrapping 2) Syringes placed in the syringe set without being capped or covered 3) Syringes put back in the original sterile wrapping	Patients and their environment (colonization status unknown)	Syringe hub, syringe content, and first drop from syringe	1) 102 2) 116 3) 101	1) 27% 2) 23% 3) 14%	Swab, drop on agar, and broth in syringe
Ilmarinen et al (2012)[26] Score: 90%	HPV	Outpatient clinic (Finland)	Nonstandardized	Topical application of lidocaine and prilocaine cream and CO2 laser treatment of urethral warts	Patients with HPV	Gloves	5	100%	PCR
Jeske et al (2007)[18] Score: 80%	Undifferentiated bacteria	Operating rooms (Austria)	Standardized	1-minute phone call	Hospital environment 1) Personal cell phone 2) Fixed wall phone	Hands	1) 40 2) 40	1) 95% (10% human pathogens) 2) 83% (10% human pathogens)	Contact plate
Loftus et al (2011)[32] Score: 80%	Undifferentiated bacteria	Operating room (USA)	Nonstandardized	General anesthesia	1) HCP, patients, and their environment 2) HCP	a) Valve and agent dial on the anesthesia machine b) IV stopcock set	164	1a) 89% 1b) 10% 2a) 12% 2b) 5%	Swab on plate
Ludlam et al (2010)[14] Score: 60%	MRSA	Wards and ICUs (UK)	Nonstandardized	Routine patient care	Patients with MRSA and their environment	MRSA-negative surfaces of patients with MRSA and their environment	24 audited episodes	In 38% of audited episodes at least 1 transfer occurred (2-step transfer via hands)	Swabs, culture medium unknown
Morgan et al (2012)[29] Score: 100%	MRSA VRE MDR *Acinetobacter baumanii* MDR *Pseudomonas aeruginosa*	ICU (USA)	Nonstandardized	Routine, nonemergent patient care	Patients with MRSA, VRE, MDR *A. baumanii* or MDR *P. aeruginosa* and their environment	Gloves Gowns Hands after glove removal	MRSA: 152 VRE: 180 MDR PA: 86 MDR AB: 167	MRSA: Gloves: 11% Gown: 4% Gloves or gown: 14% Hands after glove removal: 3% VRE Gloves: 10% Gown: 5% Gloves or gown: 14% Hands after glove removal: 2% MDR *P. aeruginosa:* Gloves: 17% Gown: 2% Gloves or gown: 17% Hands after glove removal: 4% MDR *A. baumanii* Gloves: 39% Gown: 13% Gloves or gown: 33% Hands after glove removal: 4%	Swab in broth
Morgan et al (2010)[28] Score: 100%	MDR *A. baumanii* MDR *P.s aeruginosa*	ICU (USA)	Nonstandardized	Routine, Nonemergent patient care	Patient with MDR *P. aeruginosa* and/or MDR *A. baumanii* and their environment	Gloves Gowns Hands after glove removal	MDR AB: 199 MDR PA and AB: 134	MDR *A. baumanii*: Gloves: 36% Gown: 11% Gloves or gown: 39% Hands after glove removal: 5% MDR *P. aeruginosa*: Gloves: 7% Gown: 5% Gloves or gown: 8% Hands after glove removal: 1%	Swab in broth

Table 1. *(Continued)*

Author (Year of Publication) Quality Score	Microorganism	Study Setting	Standardized vs Nonstandardized Interactions[a]	Interactions (Behavior)	Origin Surface[b]	Destination Surface[c]	Sample Size	Frequency of Contamination After Interaction	Microbiological Sampling Method
Ohara et al (1998)[21] Score: 90%	Staphylococci	NA (Japan)	Nonstandardized	Performing ultrasonography	Patients with MRSA	Ultrasound probe	3	100%	Swab on plate
Ojajarvi et al (1980)[15] Score: 70%	a) *S. aureus* b) Gram-negatives	Hospital, ward type not specified (Finland)	Nonstandardized	1) Making patients bed (= dry contamination) 2) Changing dressings and compresses (= wet contamination)	Patients with *S. aureus* or Gram-negatives and their environment	Hands	1) Dry contamination: 285 2) Moist contamination: 313	1a) > 90% 1b) "Small percentage" 2a) >90% 2b) 50%	Contact plate
Olsen et al (1993)[34] Score: 70%	Gram-negative rods or Enterococci	Hospital (ward type not specified) (USA)	Nonstandardized	1) Oral and endotracheal tube care for intensive care patients 2) Patient care involving digital stimulation of the rectal sphincter 3) Routine dental examinations	Patients (colonization status unknown)	Gloves Hands after glove removal	1) 98 2) 21 3) 18	Gloves: 64% (pooled for all behaviors) Hands after removal of gloves: 8% (pooled for all behaviors)	Glove juice
Pessoa-Silva et al (2004)[35] Score: 91%	Undifferentiated bacteria and fungi Skin flora Enterobacteriaceae *S. aureus* Filamentous fungi	Neonatal nursery (Switzerland)	Nonstandardized	Neonatal patient care	Neonate patients and environment (colonization status unknown)	Hands Hands after glove removal	Hands: 398 Hands after glove removal: 31	Hands: Any bacteria or fungi: 91% Skin flora: 66% Enterobacteriaceae: 14% *S. aureus*: 3% Filamentous fungi: 2% Hands after glove removal: Any bacteria or fungi: 31% Skin flora: 84% Enterobacteriaceae: 13% *S. aureus*: 3%	Contact plate
Pittet et al (1999)[2] Score: 91%	Undifferentiated bacteria *S. aureus* Gram-negative bacilli	8 different wards (Switzerland)	Nonstandardized	Routine patient care	Patients and their environment (colonization status unknown)	Hands	417	Any bacteria: 89% *S. aureus*: 9% Gram-negative bacilli: 13%	Contact plate
Ray et al (2002)[19] Score: 90%	VRE	Nursing home and hospital (USA)	Standardized	Touch bedrail and bedside table for 5 seconds each	Environment of patients with VRE	Gloves	13	46%	"Wash" gloves in broth
Rock et al (2014)[37] Score: 100%	*Klebsiella* KPC *Klebsiella* non-KPC	ICU (USA)	Nonstandardized	Routine patient care	Patients with *Klebsiella* and their environment	Gowns or gloves	*Klebsiella* KPC: 96 *Klebsiella* non-KPC: 124	*Klebsiella* KPC: 10% *Klebsiella* non-KPC: 17%	Swab in broth
Roghmann et al (2015)[30] Score: 91%	MRSA	Nursing homes (USA)	Nonstandardized	Routine patient care	Patients with MRSA and their environment	Gowns Gloves	954	Gowns: 14% Gloves: 24%	Swabs on agar and in broth

Sanderson et al (1992)[38] Score: 80%	Coliforms	Orthopedic ward Spinal injury ward (UK)	Nonstandardized	Routine patient care 1) Overall 2) Bed making 3) Touching patients or patient's clothing 4) Handling patient's wash cloth, towels or wash bowls 5) Handling used linen 6) Handling clean linen 7) Sluice room, urinary catheters or bags 8) Handling curtains or bedside furniture 9) Doing drug round	Patients or their environment (colonization status unknown)	Hands	452	Orthopedic ward/spinal injury ward 1) 20%/36% 2) 13%/20% 3) 32%/32% 4) 57%/62% 5) 6%/22% 6) 0%/29% 7) 15%/26% 8) 23%/12% 9) 13%/27%	Contact plate
Snyder et al (2008)[25] Score: 91%	MRSA VRE	ICU (USA)	Nonstandardized	Routine, nonemergent patient care	Patients with MRSA and/or VRE and their environment	Gowns Gloves Hands after glove removal	137	MRSA: Gloves: 18% Gowns: 6% Gloves or gowns: 19% Hands after glove removal: 3 VRE: Gloves: 8% Gowns: 4% Glove or gown: 9% Hands after glove removal: 0%	Swab on agar and swab in broth
Stiefel et al (2011)[44] Score: 100%	MRSA	Hospital, ward type not specified (USA)	Standardized	Imprint gloved hand on 1) Patients skin (abdomen, chest, hand, and arm) 2) Patients environment (call button, bed rail, table, and phone)	Patients with MRSA or their environment	Gloves	40	1) 40% 2) 45%	Contact plate
Tenorio et al (2001)[36] Score: 91%	VRE	Hospital, ward type not specified (USA)	Nonstandardized	Routine patient care	Patients with VRE and their environment	Gloves Hands after glove removal	44	Gloves: 39% Hands after glove removal: 14%	"Wash" hands or gloves in broth
Zachary et al (2001)[22] Score: 91%	VRE	Hospital, ward type not specified (USA)	Standardized	Structured physical examination (auscultation of heart and lungs, palpation of back, abdomen, and lower extremities)	Patients with VRE and their environment	Hands Gowns Stethoscope diaphragms	49	Glove, gown, or stethoscope: 67% (Gloves: 63%; gowns: 37%; stethoscope diaphragms: 31%)	Contact plate

Note. HCP, healthcare practitioner; HPV, human papilloma virus; ICU, intensive care unit; KPC, *Klebsiella pneumonia* carbapenemase; NA, not applicable; MDR, multidrug resistant; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; UK, United Kingdom; USA, United States of America; VRE, vancomycin-resistant Enterococci.

[a]In standardized interactions, the interaction was standardized by role playing; in nonstandardized interactions, the interactions were observed in real life.

[b]Surface *from* which pathogen was transferred.

[c]Surface *to* which pathogen was transferred.

Table 2. Summary and Quality Assessment for Studies Reporting Quantity of Contamination

Author (Year of Publication) Quality Score	Microorganism	Study Setting	Standardized vs Nonstandardized Interactions[a]	Standardized Interactions	Origin Surface[b]	Destination Surface[c]	Sample Size	No. of CFU transferred	Microbiological Sampling Method
Guerrero et al (2012)[46] Score:100%	*C. difficile*	NA (USA)	Standardized	Touch 1) Commonly examined skin sites (arm, abdomen, chest, and hand) 2) Environment (table, phone, bedrail, and call button)	Patients with *C. difficile* and their environment	Moistened gloves	30	CFU on handprint (mean): 1) 14 (highest CFU count after touching Abdomen: 29) 2) 7 (highest CFU count after touching bedrail: 8)	Contact plate
Hamburger et al (1947)[52] Score: 90%	Beta-hemolytic streptococci	NA (USA)	Standardized	Handshake	Sailors with beta-hemolytic streptococci 1) Hands after nose blowing 2) Hands without blowing nose	Hands	1) 17 2) 9	CFU on hand (mean) 1) 4450 2) 564	“Broth wash”
Jeske et al (2007)[18] Score 80%	Undifferentiated bacteria	Operating rooms (Austria)	Standardized	One-minute phone call	“Hospital environment” 1) Cell phone 2) Fixed wall phone	Hands	1) 40 2) 40	CFU on 5 fingertips (median) 1) 14 2) 22	Contact plate
Longtin et al (2014)[4] Score: 100%	1) Aerobic bacteria 2) MRSA	Ward (Switzerland)	Standardized	Standardized physical examination	Patients colonised or infected with MRSA and their environment	Stethoscope gloves Hands	1) 33 2) 50	CFU per $25cm^2$ (median) 1) Fingertips: 467 Stethoscope diaphragm: 89 Thenar/hypothenar: 37 Stethoscope tube: 18 Dorsum hand: 8 2) Fingertips: 12 Stethoscope diaphragm: 7 Thenar: 7 Hypothenar: 2 Stethoscope tube: 0 Dorsum hand: 0	Contact plate
Olsen et al (1993)[34] Score: 70%	Gram-negative rods or Enterococci	hospital, ward type not specified (USA)	Nonstandardized	“Moist” interactions 1) Oral and endotracheal tube care for intensive care patients 2) Patient care involving digital stimulation of the rectal sphincter 3) routine dental examinations	Patients and their environment (colonization status unknown)	Gloves Hands after glove removal	1) 98 2) 21 3) 18	CFU on glove or on hand after glove removal: Glove: 650–2,000,000 Hand after glove removal: 10–100	Glove juice
Pessoa-Silva et al (2004)[35] Score: 91%	Undifferentiated bacteria and fungi	Neonatal nursery (Switzerland)	Nonstandardized	Neonatal patient care	Neonate patients and environment (colonization status unknown)	Hands	149	Increase in CFU on 5 fingertips per minute: Total: 20 skin contact: 21 Diaper change: 42 Respiratory tract care: 38 Contact with body secretions other than respiratory: 20 Manipulation of vascular access	Contact plate

								devices: 10 Contact with equipment: 9	
Pittet et al (1999)[2] Score: 91%	Undifferentiated bacteria	8 different wards (Switzerland)	Nonstandardized	Patient care	Patients and their environment (colonization status unknown)	Hands	417	CFU on 5 fingertips: 100 (mean), 39 (median) Increase in CFU on 5 fingertips per minute: Overall: 16 Direct patient contact: 20 Rupture in the sequence of care: 19 Respiratory care: 21 Handling body fluid Secretions: 16 Blood sampling and intravenous injection of care: 6 Skin contact: 4	Contact plate
Stiefel et al (2011) [44] Score: 100%	MRSA	Hospital, ward type not specified (USA)	Standardized	Imprint gloved hand on 1) Patients skin (abdomen, chest, hand, and arm) 2) Patients environment (call button, bed rail, table, and phone)	Patients with MRSA and their environment	Gloves	40	CFU on hand imprint (mean) 1) Touching patients skin (any): 9 (highest CFU count after touching Abdomen: 17) 2) Touching patients environment (any): 4 (highest CFU count after touching call button: 6)	Contact plate
Tschopp et al (2016) [23] Score: 91%	Undifferentiated bacteria	Normal wards (Switzerland)	Standardized	Standardized physical examination	Patient and or his environment (colonization status unknown)	Hand (fingertips, dorsum, thenar and hypothenar) Stethoscope (tube and diaphragm)	56	CFU per 25 cm^2 (median)ngertips: 834 Stethoscope diaphragm: 172 Stethoscope tube: 116 Thenar: 14 Hypothenar: 16 Dorsum hand: 2	Contact plate

Note. CFU, colony-forming unit; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not applicable; UK, United Kingdom; USA, United States of America.
[a]In standardized interactions, the interaction was standardized by role playing; in nonstandardized interactions, the interactions were observed in real life.
[b]Surface *from* which pathogen was transferred.
[c]Surface *to* which pathogen was transferred.

Table 3. Summary and Quality Assessment for Studies Reporting Risk Factor Analysis

Author (Year of Publication) Quality Score	Microorganism	Study Setting	Interactions	Origin Surface[a]	Destination Surface[b]	Risk Factors for Transfer
Bache et al (2013)[31] Score: 91%	*Staphylococci*	Burns ICU (UK)	Dressing change with or without bed making	Patients and their environment (colonization status unknown)	Gown	For every 9% increase in total body surface area of burn: CFU/plate double
Hayden et al (2008)[43] Score: 100%	VRE	ICU (USA)	Patient care 1) Touching patient and environment 2) Touching only environment	Patients with VRE and their environment	Hands or gloves	Positive predictors for contamination (univariable analysis): - No. of contacts made (each contact results in 10% risk of hand contamination) Independent positive predictors for contamination: - None
Morgan et al (2012)[29] Score: 100%	MRSA, VRE, MDR *Acinetobacter baumanii*, MDR *P. aeruginosa*	ICU (USA)	Patient care	Patient with MRSA, VRE, MDR. *A. baumanii*, or MDR *P. aeruginosa* and their environment	Gloves Gowns Hands after glove removal	Independent positive predictors for contamination: - Positive environmental culture (OR, 4.15) - Time in room of more than 5 minutes - Performing a physical examination (OR, 1.74) - Contact with the ventilator (OR, 1.78)
Morgan et al (2010)[28] Score: 100%	MDR *Acinetobacter baumanii* MDR *Pseudmonoas aeruginosa*	ICU (USA)	Patient care	Patient with MDR *P. aeruginosa* and/or MDR. *A. baumanii* and their environment	Gloves Gowns Hands after glove removal	Independent positive predictors for contamination: - Presence of a wound dressing (OR, 25.9) - Use of endotracheal tube or tracheostomy site (OR, 2.1) - Time in room of more than 5 minutes (OR, 4.3) - Clinical role of physician or nurse practitioner (OR, 7.4) or nurse (OR, 2.3) compared to clinical role of therapists
Pessoa-Silva et al (2004)[35] Score: 91%	Undifferentiated bacteria and fungi	Neonatal nursery (Switzerland)	Routine neonatal care	Neonate patients and environment	Hands Hands after gloves were removed Gloves	Independent positive predictors for contamination: - Skin contact - Diaper change - Respiratory care - Duration of care
Pittet et al (1999)[2] Score: 91%	Undifferentiated bacteria	8 different wards (Switzerland)	Patient care	Patients and their environment	Hands	Independent positive predictors for contamination: - No hand antisepsis - Each minute spent performing patient care (direct patient contact, rupture in the sequence of care, respiratory care, handling body fluid secretions) - Patient care in medical rehabilitation compared to other wards Independent negative predictors for contamination: - Patient care in septic orthopedic surgery compared to other wards
Rock et al (2014)[37] Score: 100%	*Klebsiella* KPC *Klebsiella* NonKPC	ICU (USA)	Routine patient care	Patients with *Klebsiella* and their environment	Gowns Gloves	Positive predictors for contamination (univariable analysis): - Providing wound care - Manipulating catheter or drain - Caring for a patient with endotracheal tube or tracheostomy - Presence of a urinary catheter - Presence of endotracheal tube or tracheostomy
Roghmann et al (2015)[30] Score: 91%	MRSA	Nursing homes (USA)	Patient care	Patients with MRSA and their environment	Gowns Gloves	Positive predictors for contamination (univariable analysis): - Dressing the resident - Transferring the resident Providing hygiene (brushing teeth, combing hair) - Changing linens - Changing diapers - Patients with chronic skin breakdown Negative predictor for contamination: - Giving medications and performing glucose monitoring

Table 3. (*Continued*)

Author (Year of Publication) Quality Score	Microorganism	Study Setting	Interactions	Origin Surface[a]	Destination Surface[b]	Risk Factors for Transfer
Snyder et al (2008)[25] Score: 91%	MRSA VRE	ICU (USA)	Routine patient care	Patients with MRSA and/or VRE and their environment	Gowns Gloves Hands after glove removal	Independent positive predictors for contamination with MRSA and VRE: - Percutaneous endoscopic gastrostomy/jejunostomy tube - HCP contact with a patient's endotracheal tube or tracheostomy Independent positive predictors for contamination with MRSA: - Patient with endotracheal tube - Endotracheal tube or tracheostomy use or care - Contact with patient's head and/or neck, right lower extremity Independent positive predictors for contamination with VRE: - Catheter/drain care or use - Contact with patient's trunk, left lower extremity
Tenorio et al (2001)[36] Score: 91%	VRE	Hospital, ward type not specified (USA)	Patient care	Patients with VRE and their environment	Gloves Hands after glove removal	Positive predictors for contamination with VRE on gloves (univariable analysis): - Duration of contact - Contact with patient's body fluid - Presence of diarrhea in a patient - Mean VRE-count on patient skin - No. of patient body sites colonized with VRE
Tschopp et al (2016)[23] Score: 91%	Undifferentiated bacteria	Ward (Switzerland)	Standardized Physical examination	Patient	Hand (fingertips, dorsum, thenar, and hypothenar) Stethoscope (diaphragm and tube)	Independent predictors for contamination: - Stethoscope diaphragm: Higher bacterial count on patient's skin - Stethoscope tube: Higher bacterial count on patient's skin, male sex, reception of a bed bath rather than a shower or sink bath
Zachary et al (2001)[22] Score: 91%	VRE	Hospital, ward type not specified (USA)	Structured physical examination (auscultation of heart and lungs, palpation of back, abdomen, lower extremities)	Patients with VRE and their environment	Hands Gown Stethoscope diaphragm	Positive predictors for contamination with VRE on gloves (univariable analysis): - Presence of colostomy or ileostomy - Examination of patient by first year infectious disease fellow compared to infection control practitioners

Note. ICU, intensive care unit; KPC, *Klebsiella pneumonia* carbapenemase; NA, not applicable; MDR, multidrug resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; UK, United Kingdom; USA, United States of America; VRE, vancomycin-resistant Enterococci.
[a]Surface *from* which pathogen was transferred.
[b]Surface *to* which pathogen was transferred.

environment, (2) organism transfer to hands, (3) organism survival on hands, (4) defective hand cleansing resulting in hands remaining contaminated, and (5) contaminated hands cross transmitting organisms to the next patient. Our review examines this sequence and systematically summarizes the existing literature. Unsurprisingly, in concordance with the prevailing perception that hands are "the" vector in healthcare settings, most papers focus on pathogen transfer to hands or gloves. Hand and glove contamination after contact with patients and their environment occur in an estimated 33% and 30% of interactions, respectively. Strikingly, only 2 studies addressed the transfer to the patient (step 5 in the aforementioned concept paper), which is immediately relevant for patient safety.[14,24] Duckro et al[24] examined the transfer of VRE from positive to negative body sites of patients and surfaces in their immediate environment via hands and demonstrated a transfer frequency of 11%. Ludlam et al[14] investigated the transfer of MRSA in a similar study and found that in 38% of audited care episodes at least 1 destination surface was contaminated. With poor hand hygiene compliance before patient contact,[41] the question of transfer frequency *to* a patient is of highest interest. We suspect that due to patient safety concerns, studies on pathogen transfer from one patient to another might be limited to laboratory studies not covered by this review.

However, 4 studies did address the question of contamination frequencies of hands after glove removal. An estimated contamination frequency of 3% shows that gloves do not provide full protection against pathogens. Contamination may occur through glove microperforation or during doffing, which highlights the importance of hand hygiene after glove removal.

The hospital environment and contaminated surfaces make important contributions to the transmission of nosocomial pathogens,[42] and patients are considered the main source for environmental contamination. This review identified 2 studies investigating the transfer of VRE and MRSA to the patient environment via HCP hands.[14,24] Additionally, contamination of anesthesia machines, stopcocks, and syringes via HCP hands was studied.[32,33] The acquisition of pathogens from the patient environment to HCP hands, gloves, or gowns was the subject of many reports: HCP behaviors entailing only environmental contact led to transfer frequencies >40% for VRE, MRSA, and

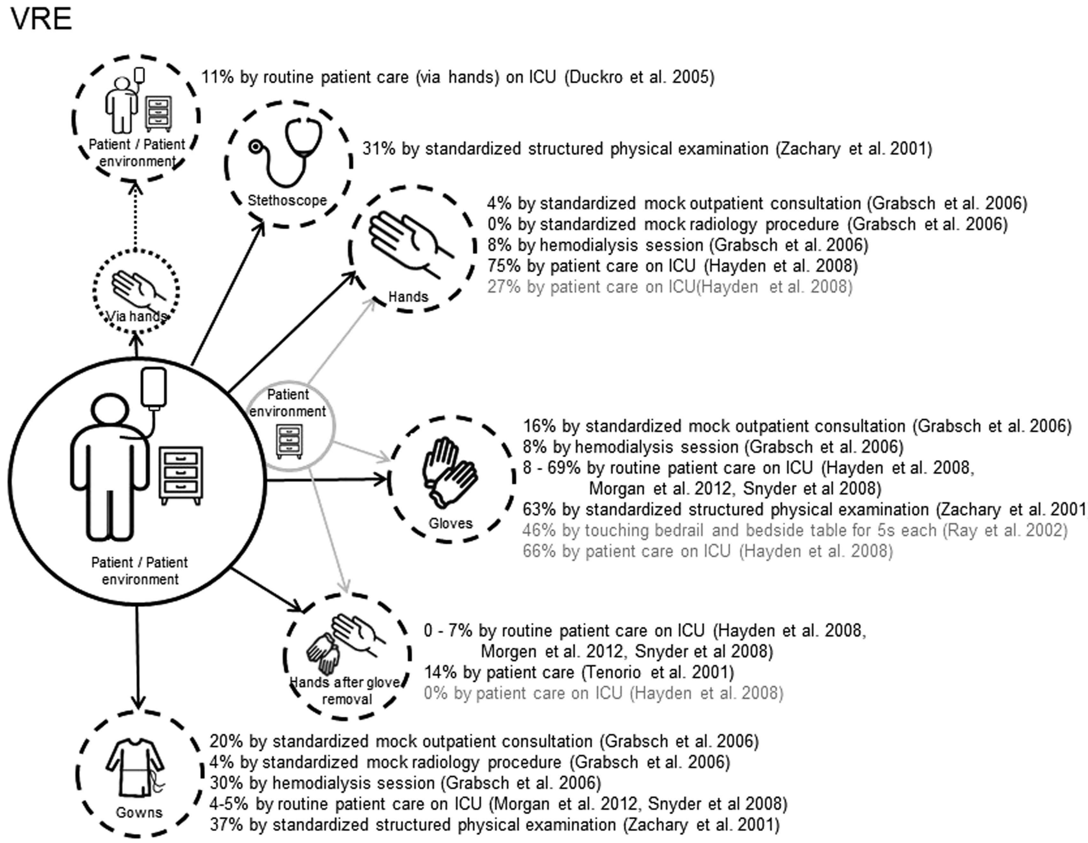

Fig. 2. Transfer frequency of VRE. Abbreviations: ICU, intensive care unit; VRE, vancomycin resistant enterococci; black circle, surface of origin, patient, and the patient environment; grey circle, surface of origin, patient environment, or inanimate objects; dotted circle, transfer surface; dashed circle, destination surface. Percentage is the transfer frequency or percentage of destination sites colonized or contaminated with corresponding microbe.

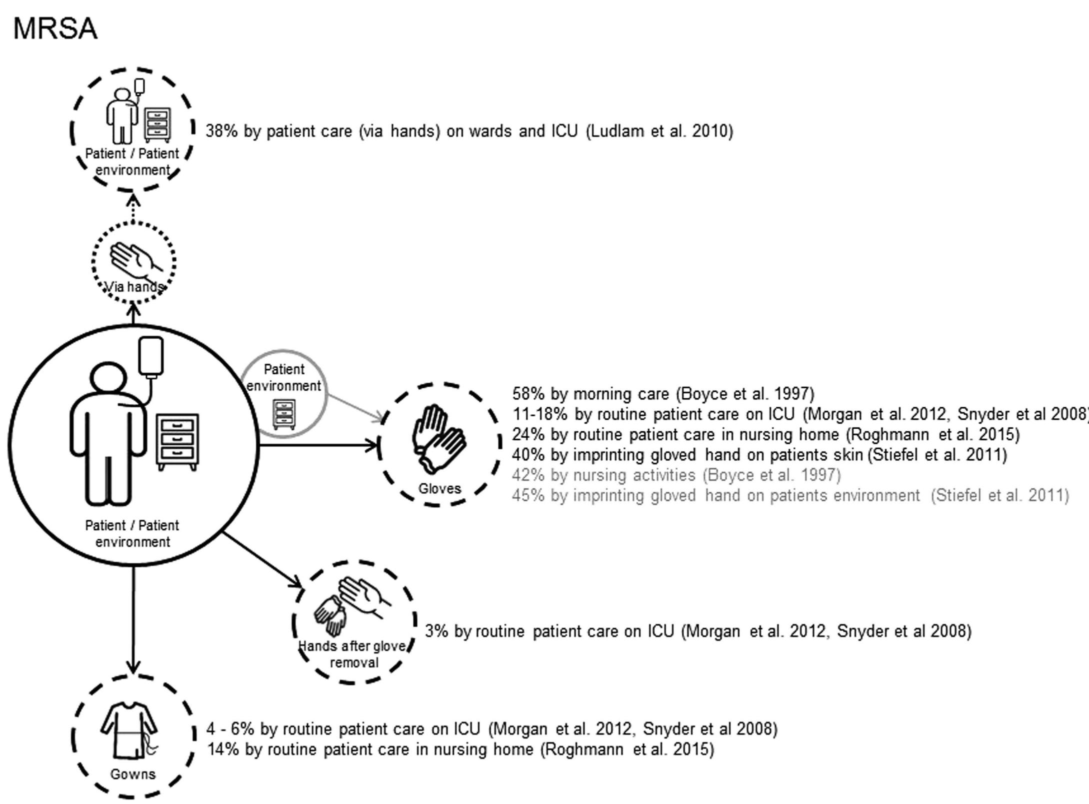

Fig. 3. Transfer frequency of MRSA. Abbreviations: ICU, intensive care unit; MRSA, methicillin-resistant *S. aureus*; black circle, surface of origin, patient, and the patient environment; grey circle, surface of origin, patient environment, or inanimate objects; dotted circle, transfer surface; dashed circle, destination surface. Percentage is the transfer frequency or percentage of destination sites colonized or contaminated with corresponding microorganism.

Clostridium difficile.[19,43–46] In conclusion, pathogen transfer to and from patient environments and noncritical medical devices occurs often. These contaminated surfaces can then act as intermediate vectors and may play an important role in transmission to patients.

Whether HCP attire plays a role in the transfer of pathogens is a topic of considerable debate and controversy. While we identified numerous studies addressing pathogen transfer to uniforms or gowns, we did not identify any study reporting transfer pathogens *from* gowns and uniforms to patients. In general, gowns became contaminated at a lower percentage than gloves or hands, but estimated proportions were still significant at 11%. Notably, a 2007 review was also not able to find conclusive evidence that contaminated uniforms act as vehicles to transfer pathogens to patients.[47]

The quantity of contamination was reported to be ~ 10–1000 CFU per 5 fingertips or hand. The single study reporting considerably higher CFU counts investigated moist interactions.[34] This finding is in line with the finding of the risk-factor analyses showing that contacts with moist body sites lead to higher frequency of transfer of pathogens.[25,28–30,35–37] Sampling technique may impact on CFU counts when studying transmission. The 2 studies reporting the highest CFU counts differed from the others by applying glove juice or "broth wash" sampling instead of the contact plate method.

Our review has several limitations. First, the studies in this review are very heterogeneous. This is partly explained by the fact that a multitude of factors influences the transfer of microorganisms such as the type of pathogen, surface characteristics (eg, moisture), frequency and intensity of contact between surfaces, and inoculum size. The number of organisms present on intact areas of patient skin is known to vary from 10^2 to 10^6 CFU/cm.[40] Moreover, several factors influence the detection of pathogens on the sampled destination surface such as microbial sampling, culture technique, and the size of the sampled surface area. A systematic review by Jullian et al[48] on hand contamination with *C. difficile* also attributed the wide range of values to the heterogeneity of study designs. Second, in 10 studies the origin surface was not sampled, in others only the colonization status of the patient with MDR pathogens was indicated but not the exact colonized body sites or the contamination status of the inanimate surfaces. Such study methods could lead to an underestimated transfer frequency because no contact with contaminated surfaces is possible in the study scenarios. Third, during multistep prolonged interactions, the exact origin of transferred microorganisms remains unknown. When the observed interaction involved patients and the environment, both can act as origin surfaces. The HCP himself may even be the origin of pathogens; for example, touching the nose is a common habit and can contaminate hands.[49] These 3 issues preclude a generalizable statement about exact transfer frequencies from the data of the 32 studies, and estimated proportions must be considered carefully. However, despite these limitations, every study provided an estimate of the transfer frequency or the level of contamination after a defined interaction in a real care setting. Furthermore, the studies closely mirrored clinical reality, where the colonization status usually remains unknown.

To the best of our knowledge, this is the first systematic review and meta-analysis to address the transfer of pathogens associated with HCP behavior. This is surprising considering that precise knowledge about pathogen transmission impacts the nature and extent of required preventive measures. In the absence of such knowledge, prevention policies must accept large safety margins to safeguard the system against the spread of MDR pathogens. Beyond binding unnecessary resources, this ambiguity from weak scientific evidence jeopardizes HCP acceptance and motivation to adhere to preventive policies.

In summary, this systematic review of behavior-related transmission of pathogens in healthcare settings unveiled a lacunar knowledge base coming from very heterogeneous studies. Often, the exact HCP behavior leading to pathogen transfer remains hidden in complex prolonged care sequences. Despite these uncertainties, the included studies each provide unique insight in the risk associated with contact between HCP and patients, their immediate environment, and mobile objects in real-life care settings. These commonalities allow the general conclusion that pathogen transfer is very frequent in healthcare settings. Risk factors for transmission are moist surfaces, the manipulation of invasive devices, and prolonged care activity. Higher CFU transfer is associated with moist surfaces. More systematic and well-reported research in this crucial area at the crossroads between microbiology and HCP behavior is urgently warranted to support optimal design of preventive policies.

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